Development of immune invisible beta cells as a cell therapy for type 1 diabetes through genetic modification of hESCs

Grant Award Details

Development of immune invisible beta cells as a cell therapy for type 1 diabetes through genetic modification of hESCs

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10559

Investigator:

Name:	Yang Xu
Institution:	University of California San Diego
Type:	PI

Disease Focus: Type 1 diabetes, Diabetes

Award Value: $2,167,200

Status: Pre-Active

Grant Application Details

Application Title: Development of immune invisible beta cells as a cell therapy for type 1 diabetes through genetic modification of hESCs

Public Abstract:

Research Objective

Development of hESC-derived pancreatic beta cells that are protected from allogeneic and autoimmune attack into a cell therapy for type 1 diabetes (T1D)

Impact

Cell therapy of T1D is challenged by immune rejection. Therefore, we will develop pancreatic progenitors derived from genetically modified hESCs that can evade allogeneic and autoimmune responses.

Major Proposed Activities

- To differentiate genetically modified hESCs into pancreatic β-cell precursors that express two immune suppressive molecules CTLA4-Ig and PD-L1
- To reconstitute immunodeficient mice with human immune system, denoted Hu-mice.
- To test whether CTLA4-Ig/PD-L1(CP)-expressing pancreatic β-cell precursors derived from hESCs can evade immune responses to foreign cells
- To develop humanized autoimmune T1D model reconstituted with pancreatic beta cells and autoimmune human immune system from the same individual
- To validate that CP-expressing pancreatic β-cells can evade autoimmune responses in T1D autoimmune model.
- To test whether CP-expressing pancreatic β-cells derived from hESCs can reverse insulin dependence in humanized T1D autoimmune model .

Statement of Benefit to California:

This proposal aims to find a cure for diabetes, which affects 2.3 million Californians and is associated with medical expenditures 2.3 times higher than in people without diabetes. An ultimate treatment for diabetes would be to transplant lost insulin-producing beta cells without need for immunosuppression therapy. This proposal will generate and test non-immunogenic beta cells derived from human embryonic stem cells as a renewable source of transplantable insulin-producing beta cells.
